UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

24/AUG/2010

MEMORANDUM

Subject:	Name of Pesticide Product:	F9114 EC Insecticide
	EPA Reg. No. /File Symbol:	279-GUEA
	DP Barcode:	D378509
	Decision No.:	433356
	Action Code:	R310
	PC Code:	129064 (zeta-cypermethrin)

From: Eugenia McAndrew, Biologist
Technical Review Branch
Registration Division (7505P)

To: Linda Deluise, RM Team 10
Insecticide Branch
Registration Division (7505P)

Applicant: FMC Corporation, Agricultural Products Group
1735 Market Street
Philadelphia, PA 19103

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
S-Cyano (3-phenoxyphenyl) methyl (+) cis/trans 3-(2, 2-dichloroehtenyl) -2, 2 dimethylcyclopropane carboxylate	9.6
Inert Ingredient(s):	90.4
Total:	100.0%

ACTION REQUESTED: The Risk Manager requests review of acute toxicity data for 279-GUEA.

BACKGROUND: FMC Corporation, Agricultural Products Group has submitted a six pack of acute toxicity studies to support the registration of the proposed product, F9114 EC Insecticide, EPA File Symbol 279-GUEA. The studies were conducted at Eurofins/Product Safety Laboratories, Dayton, New Jersey and were assigned MRID numbers 480930-02 to -07.

RECOMMENDATIONS:

The six studies are classified as acceptable.

The acute toxicity profile for F9114 EC Insecticide, EPA Reg. No. 279-GUEA, is as follows:

Acute oral toxicity	II	Acceptable	MRID 48093002
Acute dermal toxicity	IV	Acceptable	MRID 48093003
Acute inhalation toxicity	IV	Acceptable	MRID 48093004
Primary eye irritation	II	Acceptable	MRID 48093005
Primary skin irritation	III	Acceptable	MRID 48093006
Dermal sensitization	Sensitizer	Acceptable	MRID 48093007

The basic and 4 alternate CSFs dated May 18, 2010 must be reviewed and accepted by the TRB Product Chemistry Team.

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 000279-03426

PRODUCT NAME: F9114 EC Insecticide

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

SPANISH SIGNAL WORD: AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

Hazards to Humans and Domestic Animals:

Contains Petroleum Distillate.

May be fatal if swallowed. Causes substantial but temporary eye injury. Do not get in eyes or on

clothing. Avoid contact with skin. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wear protective eyewear (goggles, face shield, or safety glasses). Wear long-sleeved shirt and long pants, socks, shoes, and chemical-resistant gloves (such as Barrier Laminate, Butyl Rubber, Nitrile Rubber, Viton, Barrier Laminate, Viton, Selection Category F, G). If the Selection Category F, G gloves do not provide adequate protection for this product, the registrant should indicate a specific glove category from the EPA chemical resistance glove selection chart that will provide adequate protection.

First Aid:

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give any liquid to the person.
-Do not give anything by mouth to an unconscious person.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: May pose an aspiration pneumonia hazard. Contains petroleum distillate.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

User Safety Recommendations:

Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse.

Reviewer: Eugenia McAndrew **Date:** August 24, 2010
Risk Manager (EPA): 10

STUDY TYPE: Acute Oral Toxicity – Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

CITATION: Durando, J. (2010) Acute Oral Toxicity Up and Down Procedure in Rats with F9114. Study Number 29174. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. April 1, 2010. MRID 48093002

SPONSOR: FMC Corporation Agricultural Products Group, 701 PrincetonSouth Corporate Center, Ewing, NJ 08628

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 48093002), seven fasted, female Sprague-Dawley derived rats (age: 10-11 weeks; weight: 172-200 g; source: Ace Animals, Inc., Boyertown, Pennsylvania) were given single oral gavage doses of undiluted F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature) at dose levels of 175 mg/kg bw (3 animals), 550 mg/kg bw (3 animals) or 5000 mg/kg bw (1 animal) and observed for up to 14 days. Dosing was conducted according to AOT425statpgm. The test substance was administered as received. An initial limit dose of 5000 mg/kg was administered to one rat. Due to mortality in this animal, the study proceeded to a Main Test. Using the default starting dose of 175 mg/kg, six additional females were dosed.

At 175 mg/kg, animals survived and gained weight. One rat exhibited clinical signs of toxicity including facial staining, hypoactivity and ano-genital staining. The animal recovered from these symptoms by day 2. No gross abnormalities were noted at necropsy. At 550 mg/kg, all three animals died within one day of test substance administration. Toxic signs noted prior to death included hypoactivity, hunched posture, tremors and/or ataxia. Gross necropsy of the decedents revealed discoloration of the intestines. At 5000 mg/kg, the one animal died within one day of test substance administration. Prior to death, the animal was hypoactive and exhibited ataxia. Gross necropsy of the decedents revealed discoloration of the intestines and distention of the stomach.

LD_{50} Females = 310.2 mg/kg bw (95% confidence interval of 175 mg/kg (lower) to 550 mg/kg (upper).

Based on the acute oral LD_{50}, F9114 is in EPA Toxicity Category II.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Tuesday, August 17, 2010, 11:24:28 AM
Data file name: F9114.dat
Last modified: 8/17/2010 11:24:26 AM

Test/Substance: F9114
Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	3102	175	O	O
2	3103	550	X	X
3	3104	175	O	O
4	3105	550	X	X
5	3106	175	O	O
6	3107	550	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

Stopping criteria met: 5 reversals in 6 tests. LR criterion.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
175	3	0	3
550	0	3	3
All Doses	3	3	6

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Statistical Estimate based on long term outcomes:

Estimated LD50 = 310.2 (Based on an assumed sigma of 0.5).
Approximate 95% confidence interval is 175 to 550.
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Statistical Analysis: The Acute Oral Toxicity (Guideline 425) Statistical Program (Westat, version 1.0, May 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations, and/or LD_{50} and confidence limit calculations.

A. Mortality: At 5000 mg/kg, all animals died within five days of test substance administration.

B. Clinical observations: At 175 mg/kg, animals survived and gained weight. One rat exhibited clinical signs of toxicity including facial staining, hypoactivity and ano-genital staining. The animal recovered from these symptoms by day 2. At 550 mg/kg, all three animals died within one day of test substance administration. Toxic signs noted prior to death included hypoactivity, hunched posture, tremors and/or ataxia. At 5000 mg/kg, the one animal died within one day of test substance administration. Prior to death, the animal was hypoactive and exhibited ataxia.

C. Gross necropsy: No gross abnormalities were noted for any of the animals surviving to study termination. Gross necropsy of the decedents revealed discoloration of the intestines and/or distention of the stomach.

D. Reviewer's conclusions: In agreement with the study author, the acute oral LD_{50} for females is 310.2 mg/kg (95% PL confidence interval of 175 mg/kg (lower) to 550 mg/kg (upper). This places the test material in EPA Toxicity Category II.

Reviewer: Eugenia McAndrew **Date:** August 24, 2010
Risk Manager (EPA): 10

STUDY TYPE: Acute Dermal Toxicity – Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

CITATION: Durando, J. (2010) Acute Dermal Toxicity Study in Rats with F9114. Study Number 29175. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. April 1, 2010. MRID 48093003

SPONSOR: FMC Corporation Agricultural Products Group, 701 PrincetonSouth Corporate Center, Ewing, NJ 08628

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 48093003), a group of five male and five female Sprague-Dawley derived albino rats (age: 9-10 weeks old; weight: males: 286-338 g, females: 180-208 g source: Ace Animals, Inc., Boyertown, Pennsylvania) was dermally exposed to F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature) for 24 hours. Five thousand mg/kg of body weight of the test substance was applied to a dose area of approximately 2 inches by 3 inches (approximately 10% of the body surface) and covered with a 4-ply gauze pad. The gauze pad and entire trunk of each animal were wrapped with Durapore tape. The animals were then observed for 14 days, including observation and scoring of the dose sites for dermal irritation.

All animals survived. One male and one female lost weight through day 7 but all animals exceeded initial weights by the end of the study. All rats exhibited clinical signs including nasal discharge, hyperactivity, hunched posture and/or ano-genital staining. All rats showed signs of mechanical damage due to unwrapping and/or adhesive residue around the dose site. All animals recovered from these symptoms by day 7. Dermal irritation was noted at the dose site of one female between days 1 and 6. No gross abnormalities were noted at necropsy.

LD_{50} Males > 5000 mg/kg bw
LD_{50} Females > 5000 mg/kg bw
LD_{50} Combined > 5000 mg/kg bw

Based on the acute dermal LD_{50}, F9114 is in EPA Toxicity Category IV.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

A. **Mortality:** There were no deaths.

B. **Clinical observations:** One male and one female lost weight through day 7 but all animals exceeded initial weights by the end of the study. All rats exhibited clinical signs including nasal discharge, hyperactivity, hunched posture and/or ano-genital staining. All rats showed signs of mechanical damage due to unwrapping and/or adhesive residue around the dose site. All animals recovered from these symptoms by day 7. Dermal irritation was noted at the dose site of one female between days 1 and 6.

C. **Gross necropsy:** There were no abnormal findings.

D. **Reviewer's conclusions:** In agreement with the study author, the acute dermal LD_{50} for males, females, and the combined sexes is greater than 5000 mg/kg bw. This places the test material in EPA Toxicity Category IV.

Reviewer: Eugenia McAndrew **Date:** August 24, 2010
Risk Manager (EPA): 10

STUDY TYPE: Acute Inhalation Toxicity – Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

CITATION: Durando, J. (2010) Acute InhalationToxicity Study in Rats with F9114. Study Number 29176. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. April 1, 2010. MRID 48093004

SPONSOR: FMC Corporation Agricultural Products Group, 701 PrincetonSouth Corporate Center, Ewing, NJ 08628

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 48093004), fifteen female Sprague-Dawley derived rats (age: 9-10 weeks; weight: 286-324 g males and 209-244 g females: source: Ace Animals, Inc., Boyertown, Pennsylvania) were exposed by nose-only inhalation for 4 hours to F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature). Two levels of exposure were selected for testing. For the 2.03 mg/L level, five males and five females were chosen for the exposure. Based on the results of this exposure, only five males were chosen for the 0.52 mg/L exposure. The test substance was aerosolized as received. Exposure was on day 0, and the animals were observed for 14 days.

At the 0.52 mg/L exposure (males only), all animals survived and gained weight. Immediately following the exposure, all rats exhibited clinical signs including abnormal respiration, hypoactivity and/or hunched posture but recovered by day 2. The mass median aerodynamic diameter (MMAD) was 2.1 and 2.2 µm and the Geometric Standard Deviation (GSD) was 2.21 and 2.17 at 1.5 and 3 hours respectively. At the 2.03 g/L exposure (males and females), one male and one female were found dead upon removal from the exposure chamber. A second male was found dead 30 minutes post-exposure. Following exposure, all surviving rats exhibited clinical signs including ocular and/or nasal discharge, facial staining, abnormal respiration, hypoactivity, abnormal posture, and/or reduced fecal volume. All surviving rats recovered from these symptoms by day 7 and all survivors gained weight. The MMAD was 2.3 and 2.2 µm and the GSD was 2.11 and 2.09 at 1.5 and 3 hours respectively. Gross necropsy of the decedents revealed discoloration of the lungs. No gross abnormalities were noted for any of the animals surviving to study termination.

LC_{50} Males > 2.03 mg/L
LC_{50} Females > 2.03 mg/L
LC_{50} Combined > 2.03 mg/L

Based on the acute inhalation LC_{50}, F9114 is in EPA Toxicity Category IV.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Nominal conc. (mg/L)	Mean gravimetric conc. (mg/L)	MMAD (µm)	GSD	Mortality/Number tested		
				Males	Females	Combined
5.49	0.52	2.1, 2.2	2.21, 2.17	0/5	-	0/5
37.99	2.03	2.3, 2.2	2.11, 2/09	2/5	1/5	3/10

Test atmosphere / Chamber description: The test atmosphere was generated using a ¼ inch JCO atomizer cap, FC3 fluid cap and AC1502 air cap. Compressed air was supplied at 30 psi. The test substance was metered to the atomization nozzle through size 14 Tygon tubing using a peristaltic pump. The nose-only inhalation chamber (Mini- Nose-Only Inhalation Chamber, ADG Developments, Ltd.) had an internal volume of approximately 6.7 L.

Gravimetric Conc. (mg/L)	0.52±0.045 (range: 0.46-0.59)	2.03±0.13 (range:1.82-2.18)
Chamber Volume (L)	6.7	6.7
Total Airflow (L/min)	25.7	25.7
Temperature (° C)	20-22	20-22
Relative Humidity (%)	45-52	44-51
Time to equilibrium (minutes)	1.2	1.2

Test atmosphere concentration: Gravimetric samples were collected from the breathing zone of the animals at 6 intervals during exposure, using a vacuum pump and pre-weighed glass fiber filters. Filter papers were weighed before and after collection to determine the mass collected. This value was divided by the total volume of air sampled to determine the chamber concentration.

Particle size determination: Two samples withdrawn from the breathing zone of the animals were analyzed using an eight-stage Andersen cascade impactor to determine the particle size distribution of the test atmosphere. The mass median aerodynamic diameter (MMAD) and

distribution of the test atmosphere. The mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were determined graphically, using two-cycle logarithmic probit axes, and are given above.

A. Mortality: At the 2.03 g/L exposure (males and females), one male and one female were found dead upon removal from the exposure chamber. A second male was found dead 30 minutes post-exposure.

B. Clinical observations: At the 0.52 mg/L exposure (males only), all animals survived and gained weight. Immediately following the exposure, all rats exhibited clinical signs including abnormal respiration, hypoactivity and/or hunched posture but recovered by day 2. The mass median aerodynamic diameter (MMAD) was estimated to be 2.15 µm. At the 2.03 g/L exposure (males and females), one male and one female were found dead upon removal from the exposure chamber. Following exposure, all surviving rats exhibited clinical signs including ocular and/or nasal discharge, facial staining, abnormal respiration, hypoactivity, abnormal posture, and/or reduced fecal volume. A second male was found dead 30 minutes post-exposure. All surviving rats recovered from these symptoms by day 7 and all survivors gained weight.

C. Gross necropsy: Gross necropsy of the decedents revealed discoloration of the lungs. No gross abnormalities were noted for any of the animals surviving to study termination.

D. Reviewer's conclusions: In agreement with the study author, the four-hour inhalation exposure LC_{50} for males, females, and the combined sexes is greater than 2.03 mg/L. This places the test material in EPA Toxicity Category IV.

Reviewer: Eugenia McAndrew **Date:** August 24, 2010
Risk Manager (EPA): 10

STUDY TYPE: Primary Eye Irritation – Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

CITATION: Durando, J. (2010) Primary Eye Irritation Study in Rabbits with F9114. Study Number 29177. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. April 1, 2010. MRID 48093005

SPONSOR: FMC Corporation Agricultural Products Group, 701 PrincetonSouth Corporate Center, Ewing, NJ 08628

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 48093005), 0.1 mL of undiluted F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature) was instilled into the conjunctival sac of the anesthetized right eye of one male and two female, young adult New Zealand albino rabbits (source: Robinson Services Inc., Clemmons, North Carolina). The upper and lower lids were held shut for approximately one second. Prior to instillation, two drops of ocular anesthetic (Tetracaine Hydrochloride Ophthalmic Solution, 0.5%0 were placed into both the treated and control eye of each animal. Eyes were scored for ocular irritation according to the Draize method 1, 24, 48, and 72 hours and on days 4, 7, 10 and 14 after instillation. The anesthetized but otherwise untreated left eye of each animal served as a control, and all eyes were rinsed following fluorescein staining at the 24-hour observation.

Corneal opacity, iritis and conjunctivitis were noted in 3/3 eyes from one through 48 hours after instillation. The irritation decreased with time. Corneal opacity and iritis were still present in one eye at the observation on day 10. All eyes were free of irritation by day 14.

In this study, the formulation is severely irritating. F9114 is classified as EPA Toxicity Category II for primary eye irritation.

This study is classified as acceptable. It does satisfy the guideline requirements for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

	Number "positive"/number tested							
Observations	**Hours**				**Days**			
	1	**24**	**48**	**72**	**4**	**7**	**10**	**14**
Corneal Opacity	3/3	3/3	3/3	2/3	2/3	2/3	1/3	0/3
Iritis	3/3	3/3	3/3	2/3	2/3	2/3	1/3	0/3
*Conjunctivae:								
Redness*	3/3	3/3	3/3	2/3	2/3	1/3	0/3	0/3
Chemosis*	3/3	3/3	1/3	0/3	0/3	0/3	0/3	0/3
Discharge**	3/3	3/3	3/3	1/3	0/3	0/3	0/3	0/3

* Score of 2 or more required to be considered "positive"
** Discharge does not indicate a positive effect according to the grading scale

A. **Observations:** Corneal opacity, iritis and conjunctivitis were noted in 3/3 eyes from one through 48 hours after instillation. The irritation decreased with time. Corneal opacity and iritis were still present in one eye at the observation on day 10. All eyes were free of irritation by day 14.

B. **Results:** The Maximum Mean Total Score (MMTS) was 36.3 (by the system of Kay and Calandra) at one hour.

C. **Reviewer's conclusions:** The test material is severely irritating to the eye and is classified as EPA Toxicity Category II for ocular effects.

Reviewer: Eugenia McAndrew **Date:** August 24, 2010
Risk Manager (EPA): 10

STUDY TYPE: Primary Dermal Irritation – Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

CITATION: Durando, J. (2010) Primary Skin Irritation Study in Rabbits with F9114. Study Number 29178. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. April 1, 2010. MRID 48093006

SPONSOR: FMC Corporation Agricultural Products Group, 701 PrincetonSouth Corporate Center, Ewing, NJ 08628

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 48093006), three female young adult New Zealand albino rabbits (source: Robinson Services Inc., Clemmons, North Carolina) were dermally exposed to F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature) for 4 hours. Five-tenths of a milliliter of the test substance was applied to one intact, clipped, 6-cm^2 dose site on each animal, covered by a gauze pad secured with semi-occlusive 3-inch Micropore tape wrapped around the trunk. After the 4-hour exposure, the pads were removed and the sites were gently cleansed. The animals were observed at 30-60 minutes and 24, 48, and 72 hours and on days 7, 10 and 14 after patch removal, and any irritation at the dose sites was scored according to Draize.

Well defined erythema (grade 2) and very slight edema (grade 1) were present on 3/3 of the dose sites 30-60 minutes after patch removal. The irritation increased to moderate to severe erythema (grade 3) at 2/3 sites and slight edema (grade 2) at 3/3 sites from 24 through 48 hours. At 72 hours, well defined erythema and very slight to slight edema were noted at all sites. The irritation decreased with time. The edema resolved by day 14 but very slight erythema persisted at all sites through the end of the study on day 14. Desquamation was present al all sites between 48 hours and day 14.

F9114 is classified as EPA Toxicity Category III for primary dermal irritation.

This study is classified as acceptable. It does satisfy the guideline requirements for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Erythema/Edema

	Time after patch removal						
	Hours				Days		
Animal Number/Sex	1	24	48	72	7	10	14
3501/F	2/1	3/2	3/2	2/2	2/2	2/1	1/0
3501/F	2/1	3/2	3/2	2/2	2/2	2/1	1/0
3503/F	2/1	2/2	2/2	2/1	2/1	2/1	1/0

A. **Observations:** Well defined erythema (grade 2) and very slight edema (grade 1) were present on 3/3 of the dose sites 30-60 minutes after patch removal. The irritation increased to moderate to severe erythema (grade 3) at 2/3 sites and slight edema (grade 2) at 3/3 sites from 24 through 48 hours. At 72 hours, well defined erythema and very slight to slight edema were noted at all sites. The irritation decreased with time. The edema resolved by day 14 but very slight erythema persisted at all sites through the end of the study on day 14. Desquamation was present al all sites between 48 hours and day 14.

B. **Results:** The Primary Irritation Index (PII) was 4.0.

C. **Reviewer's conclusions:** The test material is moderately irritating and is classified as EPA Toxicity Category III.

Reviewer: Eugenia McAndrew **Date:** August 24, 2010
Risk Manager (EPA): 10

STUDY TYPE: Dermal Sensitization – Guinea Pig; OPPTS 870.2600; OECD 404

TEST MATERIAL: F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

CITATION: Durando, J. (2010) Dermal Sensitization Study in Guinea Pigs (Buehler Method) with F9114. Study Number 29179. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. April 1, 2010. MRID 48093007

SPONSOR: FMC Corporation Agricultural Products Group, 701 PrincetonSouth Corporate Center, Ewing, NJ 08628

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 48093007), twenty young adult male Hartley albino Guinea pigs (weight: 370-488 g; source: Elm Hill Breeding Labs, Chelmsford, Massachusetts) were tested with F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature) using the Buehler method. The animals were treated with 0.4 mL of the undiluted test material for the induction and with a 25% w/w mixture of the test substance in distilled water for the challenge.

Following the challenge with a 25% w/w mixture of the test substance in distilled water, 11/20 test sites showed a sensitization response (1-2) at 24 hours persisting at 10 sites at 48 hours.

Based on the results of this study, F9114 *is* a dermal sensitizer.

This study is classified as acceptable. It does satisfy the guideline requirements for a dermal sensitization study (OPPTS 870.2600; OECD 406) in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

PROCEDURE:

A. **Induction:** The dorsal area and flanks of the animals were clipped one day prior to each treatment. For each of three successive weekly inductions, 0.4 mL of the undiluted test material was applied to the left side of each animal using an occlusive 25 mm Hill Top Chamber® and secured in place with adhesive tape wrappings for six hours. Reactions were scored 24 and 48 hours post application.

B. **Challenge:** Twenty-seven days after the first induction, the animals were challenged with 0.4 mL of a 25% w/w mixture of the test substance in distilled water (highest non-irritating concentration), applied to naïve sites on the right side of each animal for 6 hours using the same procedure. Reactions were scored 24 and 48 hours post application.

C. **Naïve controls:** At challenge, a separate "naïve" group of ten previously untreated animals was also treated with 0.4 mL of the 25% w/w mixture of the test substance in distilled water Reactions were scored 24 and 48 hours post application.

RESULTS and DISCUSSION:

A. **Reactions and durations:** Very faint to moderate erythema (0.5-2) was noted at all test sites during the induction phase. Following the challenge, 11/20 test sites showed a sensitization response (1-2) at 24 hours persisting at ten sites at 48 hours. In the naïve control group, very faint erythema (0.5) was noted at 8/10 sites at 24 hours persisting at five sites at 48 hours.

B. **Positive control:** The study report included the results from a positive control study #28478 with alpha-Hexylcinnamaldehyde Technical. The study was conducted within six months of the submitted study, and the study author stated that the induction and challenge procedures used in both studies were similar. The reviewer considers the results to be appropriate.

C. **Reviewer's conclusion:** In agreement with the study author, the test material *is* a sensitizer.

1. **DP BARCODE:** D378509
2. **PC CODE:** 129064
3. **CURRENT DATE:** August 24, 2010
4. **TEST MATERIAL:** F9114 (Lot No. PL10-0029; 9.2% F2700; brown amber liquid; pH: 4.23; expiration date: February 11, 2011; expected to be stable for the duration of testing; stored at room temperature)

Study/Species/Lab Study # / Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Eurofins | Product Safety Laboratories Study #29174/April 1, 2010	48093002	LD_{50} = 310.2 mg/kg bw females	II	A
Acute dermal toxicity/rat Eurofins | Product Safety Laboratories Study #29175/April 1, 2010	48093003	LD_{50} > 5000 mg/kg bw males, females combined	IV	A
Acute inhalation toxicity/rat Eurofins | Product Safety Laboratories Study #29176/April 1, 2010	48093004	LC_{50} > 2.03 mg/L males, females combined	IV	A
Primary eye irritation/rabbit Eurofins | Product Safety Laboratories Study #29177/April 1, 2010	48093005	Severely irritating	II	A
Primary dermal irritation/ rabbit Eurofins | Product Safety Laboratories Study #29178/April 1, 2010	48093006	Moderately irritating	III	A
Dermal sensitization/guinea pig Eurofins | Product Safety Laboratories Study #29179/April 1, 2010	48093007	*Is* a sensitizer	--	A

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived